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09/623,006	08/24/2000	Patrick Tso	10738-17	5310

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Dinsmore & Shohl
1900 Chemed Center
255 East Fifth Street
Cincinnati, OH 45202

EXAMINER	
MITRA, RITA	
ART UNIT	PAPER NUMBER
1653	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/623,006	TSO ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-62* is/are pending in the application.

4a) Of the above claim(s) *13-18 and 20-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-12 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 August 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' preliminary amendment in paper #3 filed August 24, 2000 is acknowledged. Claims 2 and 3 are canceled.

Election/Restriction

Applicants' election with traverse of Group I, claims 1 and 4-12 in paper #15 filed on October 22, 2002 is acknowledged. Applicants further elect SEQ ID NO: 5, therefore, claim 19 identifying SEQ ID NO: 5 is rejoined with Group I. The traversal is on the ground(s) that claims 15-27 are dependent upon claim 1 of Group I, thus, these claims should be included within Group I. This is not found persuasive because claims 15-27 drawn to a method of inhibiting the progression of atherosclerosis in a patient comprising administering a compound of claim 1 and claim 4. Moreover, claims 15-27 identify SEQ ID NO: 1-13 respectively and each represents different structural entity. Further Applicants assert that it would not be unduly burdensome for the Examiner to examine claims 13, 14 and 28-62 with claims 1, 4-12 and 15-27. It should be noted that a search for the method of treating atherosclerosis claims would not encompass claims to the method of preventing oxidation in a lipid containing food or pharmaceuticals, and claims to the method of preventing oxidation using a cosmetic or a dermatological composition. Consequently, a search of claims directed to the method of treating atherosclerosis, the method of preventing oxidation in a lipid containing food or pharmaceuticals, and the method of preventing oxidation using a cosmetic or a dermatological composition together would constitute an undue burden.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 13-18 and 20-62 are withdrawn under 37 C.F.R. § 1.142(b) from further consideration, as being drawn to a non-elected invention. Therefore, claims 1, 4-12 and 19 are currently pending and are under examination. Applicants are requested to cancel all non-elected sequences from the claims.

Information Disclosure Statement

The information disclosure statement filed August 24, 2000 is acknowledged. The statement indicates that the references, which, are listed in the PTO-1449 form, have been submitted. However, a copy of an English translation of a foreign reference FR 2686605 has not been submitted. Therefore, this reference listed in PTO-1449 has not been considered and lined through, however, an English language equivalent document has been considered as discussed below.

Objection to Specification

The disclosure is objected to because of the following informalities:

The continuing data is missing from page 1, line 1 of the specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-12 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating conditions associated with lipid oxidation comprising administering an apolipoprotein A-IV compound as shown in the prior art (see Boguski et al, Fig. 2, page 5022, cited under 102 rejection of this office action) does not reasonably provide enablement for a method for treating conditions associated with lipid oxidation comprising administering all apolipoprotein A-IV variants. The specification does not

enable persons skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 4-12 and 19 encompass a method for treating conditions associated with lipid oxidation comprising administering an apolipoprotein A-IV compound, wherein the compound is a peptide sequence (claims 1, 4-12, 19), a derivative, analog, homolog, fragment of apolipoprotein A-IV (claim 4). The specification, however, only discloses cursory conclusions (see page 6, lines 3-6), without data to support the findings, which state that a number of novel lipid oxidation suppressant peptides, derived from apolipoprotein A-IV, have been made, these peptides possess lipid oxidation inhibiting properties which when administered orally or intravenously, can be used to decrease atherosclerosis. There are no indicia that the present application enables the full scope in view of treating conditions associated with lipid oxidation comprising administering an apolipoprotein A-IV variant as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims 3) the amount of direction or guidance presented; 4) the presence or absence of working examples; 5) the quantity of experimentation necessary; 5); 6) the predictability or unpredictability of the art; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) The nature of the invention:

The scope of the claims includes treating conditions associated with lipid oxidation comprising administering an apolipoprotein A-IV compound, wherein the compound is a peptide sequence, and a derivative, analog, homolog, fragment of apolipoprotein A-IV, but the specification does not show the treatment using these variants. Thus, the disclosure is not enabling for the reasons discussed below.

2) The breadth of the claims:

The breadth of the claims is broad and encompasses an unspecified number of variants regarding the apolipoprotein A-IV protein products as biological active derivatives, analogs, homologs and fragments, which are not specifically described or demonstrated in the specification. The specification indicates at page 6, lines 3-6 that a number of novel lipid oxidation suppressant peptides, derived from apolipoprotein A-IV, have been made, that possess lipid oxidation inhibiting properties which when administered orally or intravenously, can be used to decrease atherosclerosis. These peptides are not adequately described or demonstrated in the specification.

Claim 4 requires a functional derivative, analog, homolog and or fragment of a peptide sequence of apolipoprotein A-IV compound, therefore at least includes the amino acid sequence that has lipid oxidation inhibition activity. However, the disclosure fails to provide a description of a variant that demonstrates such activity. Therefore, as the specification fails to describe adequately the structure and function of those apolipoprotein variants, one skilled in the art would not recognize a specific utility for the variants and would not know how to use them. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed apolipoprotein variants. Although the specification outlines art-recognized procedures for producing analogs, homologs, derivatives and fragments (pages 14, 15, 21-23), this is not

adequate guidance as to the nature of functional derivatives that may be constructed. Thus, further experimentation is required to make and use the claimed invention.

3) The amount of direction or guidance presented;
4) The presence or absence of working examples; and
5) The quantity of experimentation necessary:

The claims are directed to a method of treating conditions associated with lipid oxidation comprising administering an apolipoprotein A-IV compound and variants thereof. However, the specification only indicates apolipoprotein A-IV protein effective in protection against lipid oxidation (Examples, page 39-43, Fig 1-4), there is no disclosure or description of the use of other apo A-IV protein fragments, derivatives, homologs or analogs. There are no working examples indicating the claimed methods in association with the variants. Moreover, the specification has not shown the treating conditions using these apo A-IV variants. There are no working examples of these methods in the specification. Furthermore, the specification does not provide any specific guidance on treating conditions such as the patient population, dosage, regimen, routes of administration, the time and the treatment schedule as well as the effect of the apo A-IV variants, nor indicated the expected outcome of treatment. Since the specification fails to provide sufficient guidance on the treating conditions for various apo A-IV variants, it is necessary to have additional guidance on the identities of apo A-IV variants and to carry out further experimentation to assess the effect of an apo A-IV variant, which is used for the treatment. Without more guidance from the specification it would require undue and excessive experimentation for a person having skill in the art to be able to make and use the claimed variants.

6) The predictability or unpredictability of the art:

The invention is highly unpredictable regarding the outcome of the treatment for the reasons set forth for factors 1-5.

7) The state of the prior art:

8) The relative skill of those skilled in the art:

The prior art has shown that apolipoprotein A-IV protein, is effective as endogenous inhibitor of lipid oxidation (see section below of 102 rejection), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the treating conditions such as the dosage, the time and the effect for treating conditions associated with lipid oxidation for various apo A-IV protein products to be considered enabling for variants.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable using various apolipoprotein A-IV products, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the treatment using a apolipoprotein A-IV variants.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 4, 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite as to what the effective amount of apolipoprotein A-IV is supposed to have done in the treatment of a condition (what condition?) associated (is or is not lipid oxidation the condition?) with lipid oxidation? Does the composition administered enhance or inhibit the condition or the lipid oxidation?

Claim 4 is indefinite because it is unclear what the derivatives, analogs, homologs, fragments and mixtures of apolipoprotein A-IV compounds are. It is also not clear whether the variants have the same properties of the full-length protein. Claim 4 is also indefinite for the use of "selected from the group comprising...". Markush groups are supposed to be "closed", not

"open"; and comprising is open ended language. What are the components and amounts in the mixture recited?

Claim 7 is indefinite for the use of "mixture thereof." What are the components and amounts in the mixture recited?

Claim 11 is indefinite because of the use of the phrase "from about 1 to about 1000 mg." It is unclear what is the lower and upper limit of the peptide in the composition. What is the range of about?

Claim 12 is indefinite because of the use of the phrase "from about 1 to about 3 times a day." It is unclear what is the lower and upper limit of the dose of the composition administered per day. Does one (1) includes zero if about includes –1.0? What is the range of about? There is no apparent definition in the specification that sets limits for about.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-12 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Qin et al. (The American Physiological Society, vol 274, pp H1836-H1840, 1998, IDS Ref. XP-002115083). Qin et al. teach the role of ApoA-IV as an endogenous inhibitor in protection against lipid oxidation (see Abstract). Qin et al. further demonstrated inhibition of Copper-mediated oxidation of fasting lymph by ApoA-IV (see page H1837, col 2, Fig 1), inhibition of Copper-mediated oxidation of LDL by ApoA-IV (see page H1838, col 1, Fig 2 and 3), inhibition of Macrophage-mediated oxidation of fasting lymph by ApoAIV (see page H1838, col 1, Fig 4), thus anticipating claims 1, 4-12 and 19 of instant application. Qin et al.'s ApoA-IV is considered for the apolipoprotein A-IV compound of claim 1 and dependent claims 4-12 and 19 of instant application.

Claims 1, 4-12 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Boguski et al. (Proc. Natl. Acad. Sci., USA, vol 81, pp 5021-5025, August, 1984). Boguski et al. teach an apolipoprotein A-IV from rat that contains 13 tandem repetitions of a 22-amino acid segment with amphipathic helical potential and may thus constitute lipid-binding domains (see abstract). Boguski et al. also teach a peptide having 100% sequence identity to SEQ ID NO: 5 (see alignment result, Database: PIR_73, Accession NO: LPRTA4, November 27, 1985) (claims 1, 4 and 19). This fragment is considered for the fragment of apolipoprotein A-IV of claims 1, 4 and 19 of instant application to anticipate the claimed method of treating conditions associated with lipid oxidation via administration of peptide of SEQ ID NO: 5. (claims 1, 4 and 19). Therefore, claims 1, 4 and 19 of the instant application are being anticipated by Boguski et al.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr.Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
January 10, 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600